- CAATAAAGTC CGGTACCACA ACGCGGCTTA ATTAAGGGCT AGGTCTGTAC TATTCTATGT AACTACTCAA ACCTGTTTGG TGTTGATCTT ACGTCACTTT ATAAGATACA TIGATGAGTT TGGACAAACC ACAACTAGAA TGCAGTGAAA 1 GTIATTTCAG GCCATGGTGT TGCGCCGAAT TAATTCCCGA TCCAGACATG
 - CTTCTGCAGG TATTGCTTTA TITGTAACCA TTATAAGCTG CAATAAACAA GTTGGGCCAT GGCGGCCAAG (SEQ ID NO: 1)
- CCAGCTCGAA CCGCAGCACC GAAGACGTCC ITITACGAAA TAAACACTIT AAACACTACG ATAACGAAAT AAACATTGGT AATATTCGAC GITAITTGIT CAACCCGGTA TTACACACCC AAAATGCTTT 101
 - GGCGTCGTGG 4 GGTCGAGCTT TAGCGGCGGG GAGTCTCTCG ACGGGGGCTC AATGTGTGGG ۲ × CTCAGAGAGC TGCCCCCGAG ഗ Д ρι ப ப ec AGGATCCCCG GGGAATTCCG GCATGACTCG ATCGCCGCCC Д Д W CGTACTGAGC M T R (SEQ ID NO: 2) TCCTAGGGGC CCCTTAAGGC 201 TCGACTCTAG AGCTGAGATC
- CGIGCITACI ICCAGGGCCI GCICITCICI CYGGGAIGCG GGAICCAGAG ACAITGIGGC TGTAACACCG CCTAGGTCTC GACCCTACGC 'insert starts here
 - GTAGAAGTGG Ø U ഗ J GCACGAATGA AGGTCCCGGA CGAGAAGAGA S ſτι ᆸ ы O Ø R A Y GCTGGGAGCC TGAAGGCTCC ACTCTGGCTT TGAGACCGAA ↵ 3 ↵ CGACCCTCGG ACTTCCGAGG ρι X A O CCAGATCCTA GGTCTAGGAT 301
- CAGACCGCAC GCCAGGAGGG CATCTTCACC 401 AAAGTGCTCT TTCTGGGACT GTTGGCCTTT GGGGCCCTGG CATTAGGTCT CCGCATGGCC ATTATTGAGA CAAACTTGGA ACAGCTCTGG z ₽ ជា ц M M ĸ р П H CCCCGGGACC B B TITCACGAGA AAGACCCTGA CAACCGGAAA Ĺ ď H O ×
- CGGTCCTCCC CTGGGATTTG ធា GTCTGGCGTG ď Н 501 GCAGCCGGGT GAGCCAGGAG CTGCATTACA CCAAGGAGAA GCTGGGGGAG GAGGCTGCAT ACACCTCTCA GAFGCTGATA r H Σ Ø ഗ ⊱ E A A GACGTAATGT GGTTCCTCTT CGACCCCCTC [1] ပ Ļ × ជា × ⊁ H CGTCGGCCCA CTCGGTCCTC Ø 5
- ACCCCCCTCG TACCCTTCAG GACCCTAAAC Ω 3 CTCACACCCG AAGCACTTGG CCTCCACCTC CAGGCAGCCC TCACTGCCAG TAAAGTCCAA GTATCACTCT ATGGGAAGTC ტ ,J ഗ GTCCGTCGGG AGTGACGGTC ATTTCAGGTT Ø × > ഗ Æ E A A Ø GGAGGTGGAG ,J Ħ ц GAGTGTGGGC TTCGTGAACC S A L ГIJ Д AGAGAACATC TCTCTTGTAG ហ 601
 - GCACTAGGAG TGGGGGGAGC AACAAAATCT GCTACAAGTC AGGAGTTCCC CTTATTGAAA ATGGAATGAT TGAGTGGATG ATTGAGAAGC TGTTTCCGTG CGTGATCCTC Д [L TCCTCAAGGG GAATAACTTT TACCTTACTA ACTCACCTAC TAACTCTTCG W ſЦ Ι O z Ш H Q, > O CGATGTTCAG × >-TTGTTTAGA 701

157

GACCAACCTG GATCCAGAGC AGCTGCTGGA CTGGTTGGAC CTAGGTCTCG TCGACGACCT H ы D, Ω H z GGAGGGAGCC AAACTCCAAG GGGGCTCCGC CTACCTGCCC GGCCGCCCGG ATATCCAGTG TITGAGGITC CCCCGAGGCG GAIGGACGGG CCGGCGGGCC TATAGGICAC 3 Д ഗ Ö Ø X U CCTCCCTCGG O 801 ACTGCTTCTG TGACGAAGAC ្រ O

TCCCACAAAT CCATGGCTTC GGCCCTGTCT CCGGGACAGA O Д GGGCCAGGCC TACGTGGGGC CCCGGTCCGG ATGCACCCCG K Ø O GACGATCTGT TCCGTGTCCA CTTCCGGGAG CTGCTAGACA AGGCACAGGT > Ø × Ω ᆸ GAAGGCCCTC ĸ ſĽι CCCTTTGCCT CCCTTGAGGG GGGAAACGGA GGGAACTCCC Q ш ഗ Æ [tı 224

AGGGTGTTTA × Ħ GGTACCGAAG ഗ Ħ CAATGTGGCT CACGAGCTGA GTGGGGGCTG CACCCCCGAC ပ ဖ O GTGCTCGACT **ب** 田田 GTTACACCGA K > N CCGTCCGAGG TGCCCCCAAC CATCACAGCA GGCAGGCTCC A A Ø GTAGTGTCGT ACGGGGGGTTG GACCTCCACT GCCCACCTAG CTGGAGGTGA CGGGTGGATC 1001

CAGAGCACCT TCTTGCTGAT AGAGGCCCTG ഗ x Z A A U 257

AGAACGACTA CAGTGCTACA AGCCTGGCAG ↵ , GTCTCGTGGA TCTCCGGGAC **д** GICTCIGGG GITCCICTCG ACGACICCCG CAAGGAGAGC TGCTGAGGGC R A 1 ជា O CAGAGACCCC Ω œ GAGGCATGGC CTCCGTACCG Ø ∑ () 1101 TCATGCACTG GCAGGAGGAA TTGCTGCTGG CGTCCTCCTT AACGACGACC ۲, L L ប្រ 0 AGTACGTGAC 291

GTCCGGTCGT GTCACGATGT TCGGACCGTC Ø CAGGCCAGCA E . 0 GAGTGAGGAG CTCACTCCTC ŧΠ ŧП ഗ CAGACACATG ACATTGGCTG GTCTGTGTAC TGTAACCGAC დ ჯ Н Ω I E O CAGCTGTACG AGCATTTCCG GGGTGACTAT CCCACTGATA ≻ Q O TCGTAAAGGC (z., H GTCGACATGC O L Y CTCAGGGGCG GAGTCCCCGC ഗ 1201

GACGTACGCA CTGCATGCGT x CCTACTGTAG GGATGACATC Д CTGCCTGAGA ACGCTTCCCA GCAGATCCAT GCCTTCTCCT CCACCACCCT GACGGACTCT TGCGAAGGGT CGTCTAGGTA CGGAAGAGGA GGTGGTGGGA ഗ E E CGGCGCTTTG TGCAGCTGGC CCAGGAGGCC GGTCCTCCGG SCCGCGAAAC ACGTCGACCG 1301 324

GACTGCGCCC AGTCCCAGGG CETETGGTGG GAGGCTATCT GCTCATGCTG GCCTATGCCT GTGTGACCAT GCTGCGGTGG H I Ö Ø ഗ Ø Z ы 디 Ø Ш O r J 357

CTGACGCGGG TCAGGGTCCC S CTCGGCATCA CCTTCAATGC ပ X. ₊⊐ CTCCGATAGA CGAGTACGAC CGGATACGGA CACACTGGTA Σ E > O A Y A L M L L Y O GCACACCACC O > ж > TCTCTGAAGT CAGTGCTGCC AGAGACTTCA GTCACGACGG Þ æ ഗ 1401 391

CTCCAGGAGC GAGCCGTAGT GGAAGTTACG Н r O CTIGCCGGGG TACTGCTGGT GGCCCTGGCG GTGGCCTCAG GCCTTGGGCT CTGTGCCCTG GACACGGGAC K O CCGGGACCGC CACCGGAGTC CGGAACCCGA ↵ ഗ V A S 'A L A GAACGGCCCC ATGACGACCA ۲ ۲ ₽ AAGGCACCCG TTCCGTGGGC O 1501 424

CGGAAGTGTC TCCGAGACGG ACCGTGGGGA GAGGTCCTCG GCCTTCACAG AGGCTCTGCC TGGCACCCCT O A L ⊱ ĹĽ CITTCTTGGC TCTGGGAATC GCCGTGGATG ACGTATTCCT GCTGGCGCAT CCGCACCTAC TGCATAAGGA CGACCGCGTA X L A ᅜ > Q \ D GAAAGAACCG AGACCCTTAG E E ↵ r A GTCCACGACG 1601 CAGGTGCTGC ø 457

GCGTGCCCGT GGTCACAGCA TGAGTGTAGG TAGTTGT ACCGGCGGAA GGAGTACCGA CGGGAGCAAG GGTAGGGACG GCCCTCGTTC CCATCCCTGC GIGTCIGCAG CGCACGGGCA CCAGTGTCGT ACTCACATCC ATCAACAACA TGGCCGCCTT CCTCATGGCT A A F z Н > ഗ ပ Ę CACAGACGIC Ļ () CGTACCCGCT 1701 GCATGGGCGA

GGGACAGTAC CCTACGGCGG GGATGCCGCC æ ۲, TGCACCTTTG TAGCCGTGAT GCTTGTCTTC CCAGCCATCC TCAGCCTGGA CGAACAGAAG GGTCGGTAGG AGTCGGACCT PA L V F ACGTGGAAAC ATCGGCACTA A V M ſī, ۲ TCACCAACCG AGTGGTTGGC U > > TTCTCCCTAC AGGCGGCCAT AAGAGGGATG TCCGCCGGTA æ K 1801 GCTGCGAGCC CGACGCTCGG ĸ ᇅ 524

AAGCCCACCT CCCTGTCATG TGCTICICCA GTCCCTGCTC TGCTCAGGTG ATTCAGATCC TGCCCCAGGA GCTGGGGGAC ტ 4 CAGGGACGAG ACGAGTCCAC TAAGTCTAGG ACGGGGTCCT α Д IQIL A Q V S U ρ. ACACGAGACG ACGAAGAGGT ഗ ഗ EH C) 1901 CGCCACTGCC AGCGCCTTGA TGTGCTCTGC V L O GCGGTGACGG TCGCGGAACT Ω ĸ

GGCCAGGAGG AGGAGACAAG GCAGAAGGCA GACGGAGGGG TTCGGGTGGA 2001 CAGIGGGCAT IGCCCACCTC ACTGCCACAG ITCAAGCCIT IACCCACTGI GAAGCCAGCA GCCAGCAIGI GGICACCAIC CIGCCICCC > ν Ø TGACGGTGTC AAGTTCGGAA ATGGGTGACA CTTCGGTCGT ഗ e E J H U ſτι æ Ø ۲ ۲ T A GTCACCCGTA ACGGGTGGAG Ħ

591

CGTCTTCCGT Ø CCGGTCCTCC TCCTCTGTTC ٤٠ ш ы о 0 CCTTCTGACC CACTGGGCTC TGAGCTCTTC AGCCCTGGAG GGTCCACACG GGACCTTCTA ᆸ D L GGAAGACTGG GTGACCCGAG ACTCGAGAAG TCGGGACCTC CCAGGTGTGC ഗ ţıı ٠, ធ ഗ O 2101 GGTGCCCCCA CCACGGGGGT

CGGTAGCACG ACATGCCAAG GCCATCGTGC TGTACGGTTC GCCCCGTTGC TGCTCCAGTC CGGGGCAACG ACGAGGTCAG 2201 GCCTGCAAGT CCCTGCCTG TGCCCGCTGG AATCTTGCCC ATTTCGCCCG CTATCAGTTT Ω Ω >

GACGGATGTG GTGCCTCGGG GCACCAAGGA × A H Ø P L L TTAGAACGGG TAAAGCGGGC GATAGTCAAA (H > α ξīι NLAH ACGGGCGACC 3 æ CGGACGTTCA GGGACGGGAC U Д

accaccagaaa accacgagaa gacccggact cggagatgcc tcggtggaac cacgttctgc cggaccggga ctgcctacac cacggagccc cgtggttcct TGGTGCTCTT CTGGGCCTGA GCCTCTACGG AGCCACCTTG GTGCAAGACG GCCTGGCCCT ≻ ⊢⊐ C) Ļ ٠., æ 2301 TGGTGCTCTT

691

GCATGCCTTC CTGAGCGCCC AGCTCAGGTA CTTCTCCCTG TACGAGGTGG CCCTGGTGAC CCAGGGTGGC TTTGACTACG CCCATTCCCA ACGCGCCCTC CGTACGGAAG GACTCGCGGG TCGAGTCCAT GAAGAGGGAC ATGCTCCACC GGGACCACTG GGTCCCACCG AAACTGATGC GGGTÃAGGGT Ļ لتر K K ,_ A S [14 Ø 2401

CGTGGGGCGT GGACCGACGT GATAATGGCG TTGACCGATG GCACCCCGCA CCTGGCTGCA CTATTACCGC * X H 3 ĸ d K TITGAICIGC ACCAGGGCTI CAGIICCCIC AAGGGGGGIGC IGCCCCCACC GGCCACCCAG TICCGCCACG ACGGGGGTGG CCGGTGGGTC Ø A T p., Д ρι K A V TGGTCGCGAA GTCAAGGGAG **.**.. တ ഗ ſц rk. AAACTAGACG Ω [14 2501

GOGCATCACC CGCCACTCGT ACCGCAATGG CTCTGAGGAT GGGGCCCTGG CCTACAAGCT CGCGTAGTGG GCGGTGAGCA TGGCGTTACC GAGACTCCTA CCCCGGGACC GGATGTTCGA Ω ជោ ഗ ഗ z æ ഗ H H GGCTGCCTTT GACCAGGACT GGGCTTCTGG CCGACGGAAA CTGGTCCTGA CCCGAAGACC O ഗ Ø 3 Q (1, Ø A AGGGAATCCA TCCCTTAGGT O 2501

FIG. 10

CACGACAAAT GCTCGAGAAG CGAGCTCTTC GCTGGTGGAC AGAGAGGGAC TGATTCCACC TCTCTCCCTG ACTAAGGTGG 民 CGACCACCTG Ω r < CCCAGGAGCC TCTGGATTTC AGCCAGCTGA CCACAAGGAA TCGGTCGACT GGTGTTCCTT × ĸ € ب, O ഗ GGGTCCTCGG AGACCTAAAG ĹĽ Ω ы Д ជា GCTCATCCAG ACTGGAGACG CGAGTAGGTC TGACCTCTGC 824

GTGCTGTTTA GACCCCTGG GTCTGGCAGC CTCACAGGCC AACTTCTACC CCCCACCTCC TGAATGGCTG TTGAAGATGG GGGGTGGAGG ACTTACCGAC Д P. ξīų z CTGGGGGACC CAGACCGTCG GAGTGTCCGG 4 0 ഗ L A O ᆸ Д GGTGAGCAGT CCACTCGTCA 2801 TACATGGGGC TGACCGTGTG ACTGGCACAC ATGTACCCCG

CTGCAGACTT CTCCAGAAGA CTICGCAICC CGCCAGCICA GCCCITGGAG TITGCCCAGI ICCCCTTCCT GCTGCGTGGC ഗ ഗ > ⊠ > X X

CTGGGAACAG GAGGTCTTCT GACGTCTGAA Ø CGACGCACCG O œ ۲, CGGGAACCTC AAACGGGTCA AGGGGAAGGA ÇL, Д Ø F ជោ **.**.. D, GAAGCGTAGG GCGGTCGAGT Ø Ø Q, L R I CCCCCTCTTG GGGGGAGAAC z ĮП 2901 ACGACACCAC TGCTGTGGTG 891

ATCGAGGGGG CCCGGGCAGC ATGCGCAGAG GCCGGCCAGG CTGGGGTGCA CGCCTACCCC AGCGGCTCCC CCTTCCTCTT H ſτι O A Y P TAGCICCCC GGCCCGICG TACGCGICT CGGCCGGICC GACCCCACGI > ე 4 0 O A A U ACACCTCCGG TGTGGAGGCC 3001

TGGACGGCTG ACCTGCCGAC GGAGTTGGGG TAICIGGGCC IGCGGCGCTG CTICCIGCTG GCCGICIGCA TCCIGCIGGT GIGCACITIC CICGICIGIG CICIGCIGCT CCICAACCCC Z Z CACGTGAAAG GAGCAGACAC GAGACGACGA U L V ۲ O ACGCCGCGAC GAAGGACGAC CGGCAGACGT AGGACGACCA ۲ ۲ ᇅ A V C Ą ø, ტ ATAGACCCGG រោ 3101

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ATCCCCGTGG TGATCCTTGT TAGGGGCACC ACTAGGAACA > GCTGAGTGCC CGACTCACGG ഗ Ļ CGCTACTACT GTCACCTTGA GAAACCATAG TACCCAAAGG ACCCGTAGTT GCTGGTCCTG GCGATGATGA CAGTGGAACT CTTTGGTATC ATGGGTTTCC TGGGCATCAA H O 드 r S Н O ĹĽų CGACCAGGAC GCCTCATAGT CGGAGTATCA

CGGAACCTGC GGGCCGCCCA TGCCCTTGAG ជា > A M M ν ν ᄓ ۲, 991

CCCGGCGGGT ACGGGAACTC ,, GCCTTGGACG ₽ z z GGCATTGGCG TIGAGTICAC AGTCCACGTG GCTCTGGGCT TCCTGACCAC CCAGGGCAGC AGGACTGGTG GGTCCCGTCG G α ۲ u CGAGACCCGA CCGTAACCGC AACTCAAGTG TCAGGTGCAC > II > Ę ပ н С GGCCTCTGTA CCGGAGACAT ഗ Ø 3301 1024

CATTGTAAGG TACTTCTTTG GTAACATTCC ATGAAGAAAC > ŧН CACACATTIG CCCCCGIGAC CGAIGGGGCC AICTCCACAT IGCIGGTCT GCICAIGCIT GCIGGIICCC ACTIIGACII Ω ſΞι I ഗ B G TAGAGGTGTA ACGACCCAGA CGAGTACGAA Ļ L R ഗ ,J GGGGCACTG GCTACCCCGG B B Ω GTGTGTAAAC 3401 1057

AGIGCICACG CICCIGGGCC ICCICCAIGG ACTCGIGCIG CIGCCIGIGC IGCIGICCAI CCIGGGCCCG CCGCCAGAGG IGAIACAGAI TCACGAGTGC GAGGACCCGG AGGAGGTACC TGAGCACGAC GACGGACACG ACGACAGGTA GGACCCGGGC GGCGGTCTCC ACTATGTCTA > د r V G L / L H r L CGGCGCTGAC GCCGCGACTG 3501

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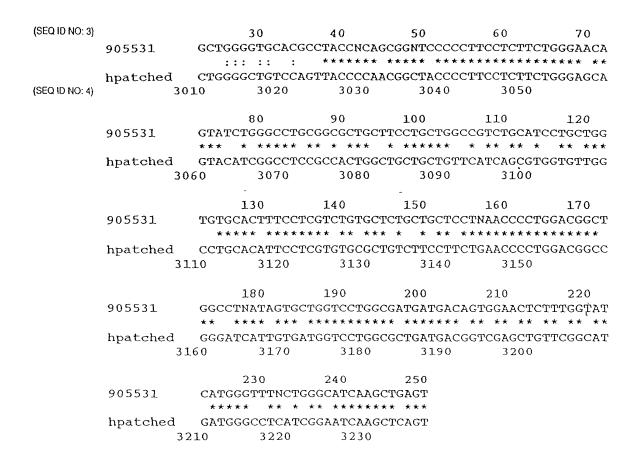
1091

3801 CTGGCANCCT CAGTTCCAGG GGACCAGGTC CAGCCACTGG GTGAAAGAGC AGCTGAAGCA CAGAGACCAT GTGTGGGGCG TGTGGGGTCA CTGGGAAGCA GACCGTTGGA GTCAAGGTCC CCTGGTCCAG GTCGGTGACC CACTTTCTCG TCGACTTCGT GTCTCTGGTA CACACCCCGC ACACCCCAGT GACCCTTCGT 3701 ACTACCTCCA TGACCGTGGC CATCCACCCA CCCCCCTGC CTGGTGCCTA CATCCATCCA GCCCCTGATG AGCCCCCTTG GTCCCCTGCT GCCACTAGCT 3601 GTACAAGGAA AGCCCAGAGA TCCTGAGTCC ACCAGCTCCA CAGGGAGGCG GGCTTAGGTG GGGGGCATCO TCCTCCCTGC CCCAGAGCTT TGCCAGAGTG CATGITCCIT TCGGGTCTCT AGGACTCAGG TGGTCGAGGT GTCCCTCCGC CCGAATCCAC CCCCCGTAGG AGGAGGGACG GGGTCTCGAA ACGGTCTCAC TGATGGAGGT ACTGGCACG GTAGGTGGGT GGGGGGGACG GACCACGGAT GTAGGTAGGT CGGGGACTAC TCGGGGGAAC CAGGGGACGA L S P ρ،

3901 CTGGGTCTGG TGTTAGACGC AGGACGGACC CCTGGAGGGC CCTGCTGCTG CTGCATCCCC TCTCCCGACC CAGCTGTCAT GGGCCTCCCT GATATCGAAT GACCCAGACC ACAATCTGCG TCCTGC GGACCTCCCG GGACGACGAC GACGTAGGGG AGAGGGCTGG GTCGACAGTA CCCGGAGGGA CTATAGCTTA

of to C (silent)

4001 TCAATCGATA GAACCGAGGT GCAGTTGGAC AGITAGCIAI CITGGCICCA CGICAACCIG



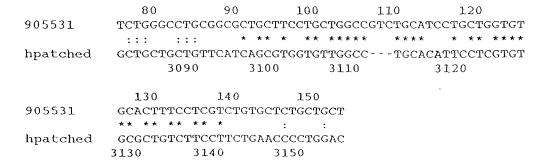
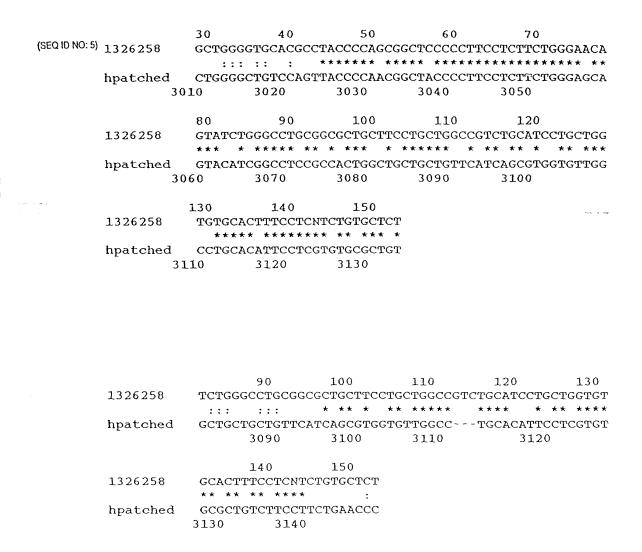


FIG. 2A



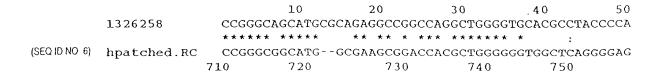


FIG. 2B

0 Y L E L . P D B A Q A A TGGLRRA Œ α Œ α ഠ A G G (۵. Œ ഗ GAP (_ ၁၅ တ G Q QDRGG a. MASAGNAAE (SEQ ID NO:2) PTCH2 SEQ ID NO:4) PTCH

IPSYCDAAFALEQISKGKATGRKAPLWLRAKFORLLFKLGCYIOKNCGK PSYTPP - - ARTAAPQILAGSLKAPLWLRAYFOGLLFSLGCGLORHCGK α ۵ エ 51 PTCH2 FLVVGLL IFGAFAVGLKAANLETNVEELWVEVGGRVSRELNYTROKIGEE VLFLGLLAFGALALGLRMAIIETNLEOLWVEVGSRVSOELHYTKEKLGEE 101 PTCH2

AMFNPOLMIOTPKEEGANVLTTEALLOHLDSALOASRVHVYMYNROWKLE AAYTSQMLIOTAROEGENILTPEALGLHLOAALTASKVOVSLYGKSWDLN 151 PTCH2

(O) HLCYKSGELITETGYMDQIIEYLYPOLTITPLDCFWEGAKLOSGTAYLL Kicyksgvpli<u>E</u>Ngmiewm<u>ie</u>klfpcviiltplocfwegakloggsaylp 158 201 PTCH2

KPPLRWTNFOPLEFLEELKKINYQVDSWEEMLNKAEVGHGYMDRPCLNPA RPDIOWTNLOPEQLLEELGPFA.SLEGFRELLDKAQVGQAYVGRPCLHPD PTCH2

ഗമ DPDCPATAPNKNSTKPLDMALVLNGGCHGLSRKYMHWQEELIVGGTVKN DLHCPPSAPNHHSRQAPNVAHELSGGCHGFSHKFMHWQEELLLGGMARDF 257 PTCH2

TGKLVSAHALOTMFOLMTPKOMYEHFKGYEY)VSH.TNWNEDKAAAILEAW OGELLRAEALOSTELLMSPROLYEHFRG.DYOTHDIGWSEEOASTVLOAW 351 307 PTCH2

RRTYVEVVHQSVAQNSTQKVLSFTTTTLDDILKSFSDVSVIRVASGYLLM RRFVQLAQEALPENASQQIHAFSSTTLDDILHAFSEVSAARVVGGYLLM 00 356 400

FIG. 3A

TM3 LAYACLTMLRWDCSKSOGAVGLAGVLLVALSVASGLGLCALLGITFNAAT LAYACVTMLRWDCAQSOGSVGLAGVLLVALAVASGLGLCALLGITFNAAT PTCH2

TM4 LALGVGVDOVFLLAHAFIEALPG - TPLQERMGECLQRTGTSVA LALGIGVDDVFLLAHAFTEALPG - TPLQERMGECLQRTGTSVV TOVLPFL 200 456 PTCH2

O W J S

တ တ р У T ഗ LYRREDRRLD | FCCF|TSPCVSRVIOVEPOAYTDTHONTRYSPPPPYS 554 504 009 PTCH2 PTCH2

ပေဖ РАНЕТОІТМОЅТVОLЯПЕУОРНТНУУУПТАЕРЯЅЕІЅVОРVТVТОПТЫЅ! PTCH2

പഗ) SPESTSSTRDLLSOFSDSSLH - - OLEPPOTKWTLSSFAEKHYAPFLLK F LFSPGGSTRDLLGOEEETROKAACKSLPOARWNLAHFARYOFAPLLLOS о п г 700 634 PTCH2

TM7

*** KAKV VV I FLFLGLLGVSLYGTTRVRDGLDLTD I VPRETREYDF I AAOFKY

**** HAKA IVLVLEGALLGLSLYGATLYODGLALTD VV PRGTKEHAFLSAOLRY PTCH2

SFYNMY IVTOKA - DYPNIOHLLYDL HRSFSNVKYVMLEENKOLPKMWL H SLYEVALVTOGGFDYAHSORALFDLHORFSSLKAVLPPPATOAPRTWLH և և

FIG. 3B

م ما X m AYKLLIVOTGSRD AYKLLIOTGDAQI DGVLA YFRDWLQGLQDAFDSDWETGKTMPNNYKNGSD YYRRNWLQGIQAAFDQDWASGRLTRHSYRNGSEL

0 0 H O ID ISQLTKORLVDADGIINPSAFYIYLTAWVSNDPVAYAASQANIRP LDFSQLTTRKLVDREGLIJPPELFYMGLTVWVSSDPLGLAASQANFYP PTCH PTCH2

(C (C) ჯ ე > ≼ EWVHOKADYMPETRLRIPAAEPIEYAOFPFYLNGLRDTSOFVEAIEI EWLHOKYD - TTGEN<u>LRIPPAOPLEFAOFPF</u>ILRGLOKIJADFVEAIE 947

TM8
FLFWEQY | GLRHWLLTF1SVVTACTFLVCALF SSYPNGYPF AAYPSGSPF I O S N Y T S L G L S : A O A E A G Q A G V H / PTCH2

The the GVE GVE TM9

LENPWTAGIIVMVLALMTVELFGMMGLIGIKLSAVPVVILIASVGI TM10

டடட шІ လ လ ပြ ပ TM11
1097 TVHVAL AFLTA IGDKNRRAVLALEHMFAPVLDGAVSTLLGVLMLAG
1033 TVHVALGELTTOGSRNLRAAHALEHTFAPVTDGA ISTLLGLLMLAG

മഗ س ب α z s а х --- ш EVSPANC EVIOMY F F G P Y P E TM12 FIVRYFFAVLAJLTHEGVLNGLVLLPVLLSF FIVRYFFAALTVLTLLGLLHGLVLLPVLLS

വ പ Oω o o ∢ ₫ ۵ ELBH AYIH шσ SOTTVSGUSE S M T V A PPSVVRFAMPPGHTHSGSDSSDS OGGGLRWGASSSLPOS - FARVTT A E م م ഗമ 1133

PTCH 1247 AGGPAHQVIVEATENPVFAHSTVVHPESRHHPPSNPRQQPHLDSGSLPP(PTCH2 1182 PWSPAATSSGNLSSRGPGPATG

Q

PTCH 1297 ROGOOPRRDPPREGLWPPLYRPRRDAFEISTEGHSGPSNRARWGPRGARS

PTCH 1347 HNPRNPASTAMGSSVPGYCQPITTVTASASVTVAVHPPPVPGPGRNPRGG

PTCH 1397 LCPGYPETDHGLFEDPHVPFHVRCERRDSKVEVIELQDVECEERPRGSSS

PTCH 1447 N

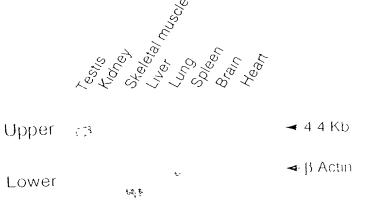


FIG. 4

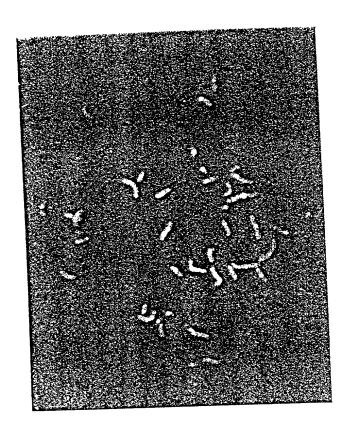
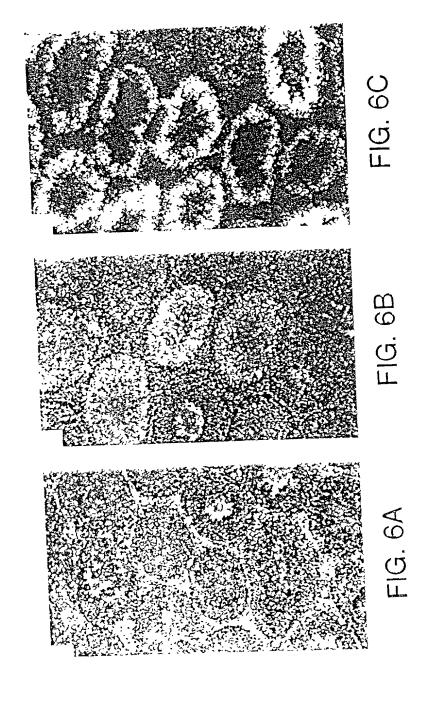
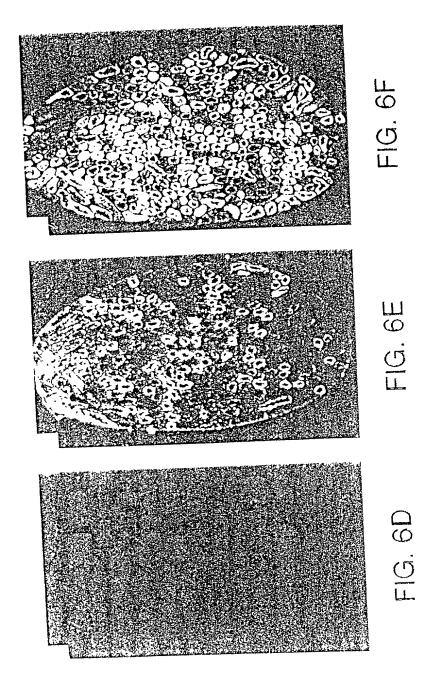
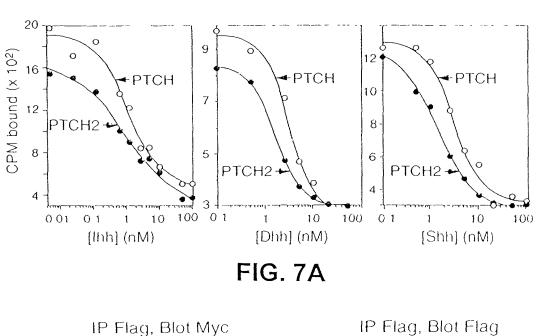


FIG. 5







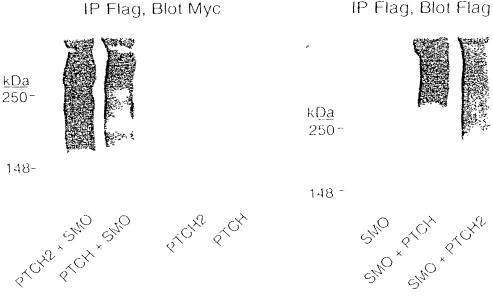


FIG. 7B

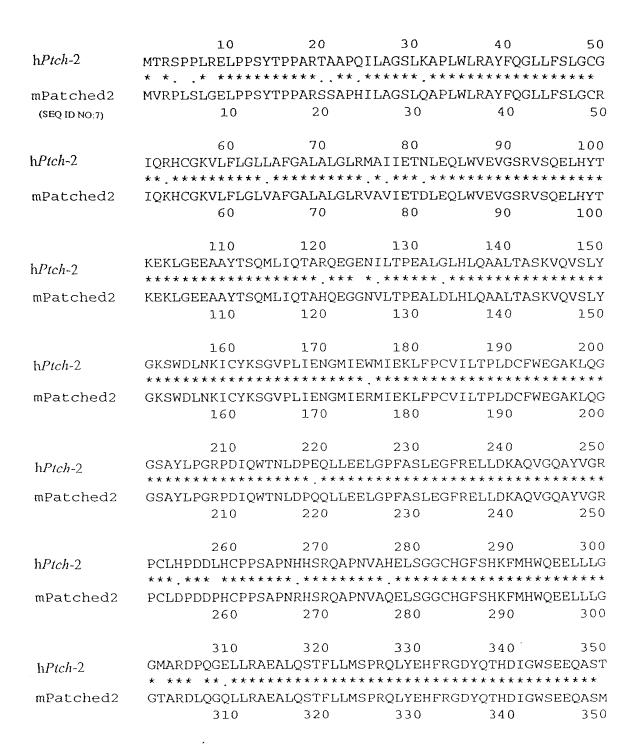


FIG. 8A

h <i>Ptch-</i> 2	360 VLQAWQRRFVQLA *******				
mPatched2	VLQAWQRRFVQLA 360	AQEALPANASQQ 370	PIHAFSSTTLI 380	DDILRAFSEVS 390	TTRVVG 400
h <i>Ptch-</i> 2	410 GYLLMLAYACVTN *******				
mPatched2	GYLLMLAYACVTN 410	1LRWDCAQSQGA 420	VGLAGVLLVA 430	ALAVASGLGLC 440	CALLGIT 450
h <i>Ptch-</i> 2	460 FNAATTQVLPFLA	*****	****	. * * * * * * * * *	* * * * *
mPatched2	FNAATTQVLPFLA 460	ALGIGVDDIFLL 470	JAHAF"I'KAPPI 480	OTPLPERMGEC 490	CLRSTGT 500
h <i>Ptch-</i> 2	510 SVVLTSINNMAA! ** ***.*** **		~		
mPatched2	SVALTSVNNMVAI 510	FFMAALVPIPAI 520	RAFSLQAAI' 530	VVGCNFAAVMI 540	VFPAIL 550
h <i>Ptch-</i> 2 mPatched2	560 SLDLRRRHCQRLI ****** *** SLDLRRRHRQRLI	************* DVLCCFSSPCS <i>i</i>	****.*** AQVIQMLPQE	*** .***** LGDRAVPVGI <i>I</i>	****** HLTATV
h <i>Ptch-</i> 2	560 610 QAFTHCEASSQH' ******				
mPatched2	QAFTHCEASSQH 610	VVTILPPQAHLI 620	LSPASDPLGS 630	ELYSPGGSTRI 640	OLLSQEE 650
h <i>Ptch-</i> 2	660 ETRQKAACKSLP	670 CARWNLAHFARY			
mPatched2	GTGPQAACRPLL				

FIG. 8B

h <i>Ptch-</i> 2 mPatched2	710 LYGATLVQDGLAL ***********************************	*****	******	****	*****
h <i>Ptch-</i> 2 mPatched2	760 HSQRALFDLHQRF ********* HSQRALFDLHQRF	*****	*****	*** . * * * * * *	****
h <i>Ptch-</i> 2 mPatched2	810 ASGRITRHSYRNG ***** ***** ASGRITCHSYRNG 810	820 SSEDGALAYKLI	830 LIQTGDAQEP:	****	850 LVDREGL ***.**
h <i>Ptch-</i> 2 mPatched2	860 IPPELFYMGLTVV ********** IPPELFYMGLTVV 860	*****	*****	*****	*****
h <i>Ptch-</i> 2 mPatched2	910 PAQPLEFAQFPFI .************************************	**.******	*****	* . * * * * * * *	*****
h <i>Ptch-</i> 2 mPatched2	960 FLFWEQYLGLRRO ******* FLFWEQYLGLRRO	****	********* CTFLVCALLL	*.******* LSPWTAGLIV	****** LVLAMMT
h <i>Pich-</i> 2 mPatched2	1010 VELFGIMGFLGIE ******* VELFGIMGFLGIE 1010	*****	**.*****	*******	. * * * * * *

FIG. 8C

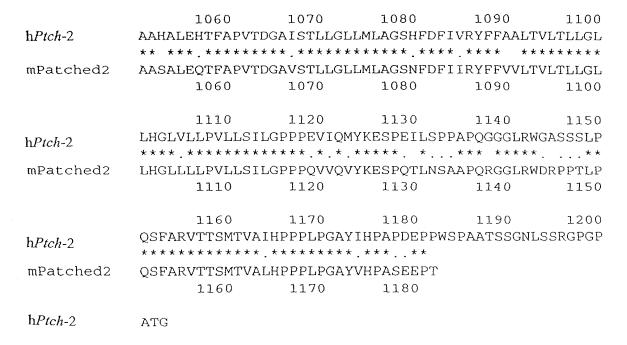


FIG. 8D

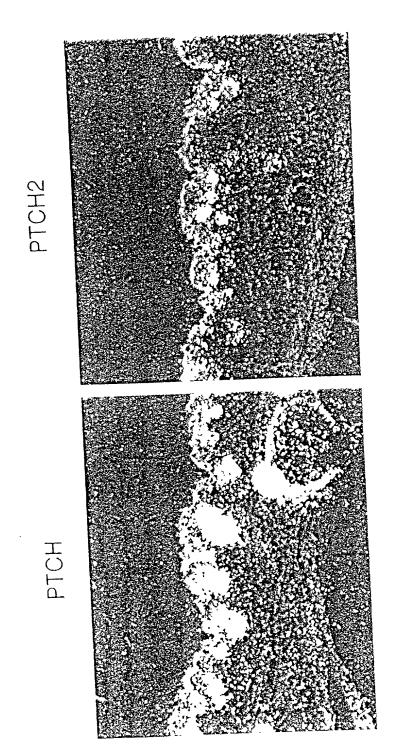


FIG. 9

> Consensus Sequence of human patched 2 cDNA clone

> length: 4004 bp

(SEQ ID NO:8)

1 CCCACGCGTC CGGGAGAAGC TGGGGGAGGA GGCTGCATAC ACCTCTCAGA TGCTGATACA GACCGCACGC CAGGAGGGAG AGAACATCCT CACACCCGAA GGGTGCGCAG GCCTTCTTCG ACCCCTCCT CCGACGTATG TGGAGAGTCT ACGACTATGT CTGGCGTGCG GTCCTCCCTC TCTTGTAGGA GTGTGGGCTT

race 5 101 GCACTTGGCC TCCACCTCCA GGCAGCCCTC ACTGCCAGTA AAGTCCAAGT ATCACTCTAT GGGAAGTCCT GGGATTTGAA CAAAATCTGC TACAAGTCAG CGTGAACCGG AGGTGGAGGT CCGTCGGGAG TGACGGTCAT TTCAGGTTCA TAGTGAGATA CCCTTCAGGA CCCTAAACTT GTT<u>TAGACG ATGTTCAGTC</u>

201 GAGIICCCCT TAITGAAAAI GGAAIGAITG AGCGGAIGAI TGAGAAGCTG TITCCGIGCG TGAICCICAC CCCCCTCGAC IGCITCTGGG AGGGAGCCAA CTCAAGGGGA ATAACTTTTA CCTTACTAAC TGGCCTACTA ACTCTTCGAC AAAGGCACGC ACTAGGAGTG GGGGGAGCTG ACGAAGACCC TCCCTCGGTT

TGAGGITCCC CCGAGGCGGA TGGACGGCGA GGGITACACC GAGIGCTCGA CTCACCCCCG ACGGTACCGA AGAGGGIGIT TAAGTACGIG ACCGICCTCC ACTECAAGGG GGETEEGEET ACCTGEEGECT ECCAATGTGG CTEAEGAGET GAGTGGGGG TGECATGGET TETECECACAA ATTEATGEAE TGGEAGGAGG

301

AATTGCTGCT GGGAGGCATG GCCAGAAGC CCCAAGGAGA GCTGCTGAGG GCAGAGGCCC TGCAGAGCAC CTTCTTGCTG ATGAGTCCCC GCCAGCTGTA TTAACGACGA CCCTCCGTAC CGGTCTTTGG GGGTTCCTCT CGACGACTCC CGTCTCCGGG ACGTCTCGTG GAAGAACGAC TACTCAGGGG CGGTCGACAT 401

GCTCGTAAAG GCCCCACTGA TAGTCTGTGT ACTGTAACCG ACCTCACTCC TCGTCCGGTC GTGTCACGAT GTTCGGACCG TCGCCGCGAA ACACGTCCAG 501 CGAGCATTIC CGGGGTGACT ATCAGACACA TGACATIGGC TGGAGTGAGG AGCAGGCCAG CACAGTGCTA CAAGCCTGGC AGCGGCGCTT TGTGCAGGTC

GGTATGGACA AGGACAGGGG GGTGCCCTGA GGCCATTCCC TCCTCCTGCC CCCTCCTATC CACCCTGTTT CTCCAGCTGG CCCAGGAGGC CCTGCCTGAG CCATACCTGT TCCTGTCCCC CCACGGGACT CCGGTAAGGG AGGAGGACGG GGGAGGATAG GTGGGACAAA GAGGTCGACC GGGTCCTCCG GGACGGACTC 601

AACGCTTCCC AGCAGATCCA TGCCTTCTCC TCCACCACCC TGGATGACAT CCTGCATGCG TTCTCTGAAG TCAGTGCTGC CCGTGTGGTG GGAGGCTATC TTGCGAAGGG TCGTCTAGGT, ACGGAAGAGG AGGTGGTGGG ACCTACTGTA GGACGTACGC AAGAGACTTC AGTCACGACG GGCACACCAC CCTCCGATAG 701

CCCCACAGCT

ACGAGTACCA CCCAGAACGT GGACCGTGGA ACGGGGGTGG GGTGGAGGTT GGTCACGGGT GGGACCCCTC GGGGACTCTG ACGGGAAAGG GGGGTGTCGA TGCTCAIGGI GGGICTIGCA CCIGGCACCI IGCCCCCACC CCACCICCAA CCAGIGCCCA CCCIGGGGAG CCCCIGAGAC IGCCCTITICC 801

FIG. 10A

23

- CCACCGGAGT GGTGGCCTCA TECTECEGIG GGACTGCGCC CAGICCCAGG GITCCGIGGG CCTIGCCGGG GIACTGCIGG IGGCCCTGGC CCGGATACGG ACACACTGGT ACGACGCCAC CCTGACGCGG GTCAGGGTCC CAAGGCACCC GGAACGGCCC CATGACGACC ACCGGGACCG GGCCTATGCC 901
 - CCGGAACCCG AGACACGGGA CGAGCCGTAG TGGAAGTTAC GACGGTGATG GGTCCATGCG GTCCTGACGT CCCGTCTGAG TCACGGTCAG TGGTCCGAAG ACCITICAATG CIGCCACTAC CCAGGIACGC CAGGACTGCA GGGCAGACTC AGTGCCAGIC ACCAGGCITIC gecerredee rerereceer 1001

CATGCCTTCA

GGTTCAAGTG

- TGCCCAGGAG TCGACGGGCG AGGACGGG GAGGTCCACG ACGGGAAGAA CTGAGACCTT TAGCCGCACC TACTGCATAA GGACGACCGC GTACGGAAGT GACTCTGGGA ATCGGCGTGG ATGACGTATT CCTGCTGGCG ACGGGTCCTC AGCTGCCGG TCCTCTGCCC CTCCAGGTGC TGCCCTTCTT 1101
- GTCTCCGAGA CGGACCGTGG GGAGAGGTCC ACCCCGGAAC AGGGGGTCCC GAGTAGACTC CGTCGAGTCG AATGACCAAT TCTCGGAGAA CCAAGTTCAC TTACTGGTTA AGAGCCTCTT CAGAGGCTCT GCCTGGCACC CCTCTCCAGG TGGGGCCTTG TCCCCCAGGG CTCATCTGAG GCAGCTCAGC 1201
- TGGAACCCGA CGAITACTIG GAGCCACGGA GAACAGGGGI ACACATTIGI CCCCTITAIT AICACGACAC AGGAITCCCA AIAACAAACC IAGICACTIC ATCAGTGAAG TATTGTTTGG ACCITGGGCT GCTAATGAAC CTCGGTGCCT CTTGTCCCCA TGTGTAAACA GGGGAAATAA TAGTGCTGTG TCCTAAGGGT 1301
 - GAACAGCCCA TCATACGTAC ATGGTACCCA ATAAATGCTA GCCACTGTGT TATGACTGCC CCACCTCTGC ACCCCAAGTT ATTGAGITCA ACTIACGAAT CITGICGGGI AGIATGCAIG TACCAIGGGI TAITTACGAI CGGIGACACA AIACTGACGG GGIGGAGACG IGGGGITCAA TAACTCAAGT 1401
- COGCCCCTCC CTTGTGACCT GAGGGCAGGT CCCCACTCTG TCCTGGCAGG AGCGCATGGG CGAGTGTCTG GGACTCGGAG GGGAAGTGAG GTGAAACTGT GCCGGGGAGG GAACACTGGA CTCCCGTCCA GGGGTGAGAC AGGACCGTCC TCGCGTACCC GCTCACAGAC CCTGAGCCTC CCCTTCACTC 1501
 - GTCGCGTGCC CGTGGTCACA ACATGAGTGT AGGTAGTTGT TGTACCGGCG GAAGGAGTAC CGACGGGAGC AAGGGTAGGG ACGCGACGCT CGGAAGAGGG CAGCGCACGG GCACCAGTGT TGTACTCACA TOCATCAACA ACATGGCCGC CTTCCTCATG GCTGCCCTCG TTCCCATCCC TGCGCTGCGA GCCTTCTCCC 1601
- ATGTOGGACO TOGATGCOGO COCOGTGACO GTOGOGGAAC TACACGAGAC GACGAAGAGO TOCATGACGO ACGOGGGGTO GGGGAAGGAG GGCACTGGGT TGCGCCCCAG CCCCTTCCTC CCGTGACCCA TACAGCCTGG ACCTACGGCG GCGCCACTGC CAGCGCCTTG ATGTGCTCTG CTGCTTCTCC AGGTACTGCC 1701
- CGCCAGCCTG ICCCCTCACC AGCATTICAA GGCACAGACC IGTCAICCAC ICTCIACCTC ITCCAGICCC IGCICTGCTC AGGIGALICA 1801
 - GGGACGGGAC AGTACCAGTG GGCATTGCCC ACCTCACTGC CACAGTTCAA GCCTTTACCC ACTGTGAAGC CAGCAGCCAG CATGTGGTCA COCTGOCÓTIG TOATGGTCAC COGTAACGGG TGGAGTGACG GTGTCAAGTT CGGAAATGGG TGACACTTCG GTCGTCGGTC GTACACCAGT GTCCTCGACC CAGGAGCTGG 1901
 - COCCACCITO TGACCCACTG GGCTCTGAGC TCTTCAGCCC TGGAGGGTCC ACACGGGACC TTCTAGGCCA GGTAGGACGG AGGGGTTCGG GTGGACCACG GGGGTGGAAG ACTGGGTGAC CCGAGACTCG AGAAGTCGGG ACCTCCCAGG TGTGCCCTGG AAGATCCGGT CCATCCTGCC TCCCCAAGCC CACCTGGTGC 2001

- 2101 GGAGGAGGAG ACAAGGCAGA AGGCAGCCTG CAAGTCCCTG CCCTGTGCCC GCTGGAATCT TGCCCATTTC GCCCGCTATC AGTTTGCCCC GTTGCTGCTC COTOCTOCTO TGITICOGICT TOOGTOGGAC GITCAGGGAC GGGACACGGG CGACOTTAGA ACGGGTAAAG CGGGCGATAG TCAAACGGGG CAACGACGAG
- STCAGTGTAC GGTTCCGGTA GCACGACCAC GAGAAGCCAC GAGAAGACCC GGACTCGGAG ATGCCTCGGT GGAACCACGT TCTGCCGGAC CGGGACTGCC CTCTTCTGGG CCTGAGCCTC TACGGAGCCA CCTTGGTGCA AGACGGCCTG CAGICACAIG CCAAGGCCAI CGIGCIGGIG CICTIIGGIG 2201

GCCCTGACGG

- TACACCACGG AGCCCCGTGG TTCCTCGTAC GGAAGGACTC GCGGGTCGAG TCCATGAAGA GGGACATGCT CCACGGGAC CACTGGGTCC CACGGAAACT CCCTGTACGA GGTGGCCCTG GTGACCCAGG GTGGCTTTGA ATGTGGTGCC TCGGGGCACC AAGGAGCATG CCTTCCTGAG CGCCCAGCTC AGGTACTTCT 2301
 - GATGCGGGTG AGGGTTGCGC GGGAGAAAT AGACGTGGTC GCGAAGTCAA GGGAGTTCCG CCACGACGGG GGTGGCCGGT GGGTCCGTGG GGCGTGGACC CCACCGGCCA CCCAGGCACC CCGCACCTGG CTACGCCCAC TCCCAACGCG CCTCTTTGA TCTGCACCAG CGCTTCAGTT CCCTCAAGGC GGTGCTGCCC 2401
- GACGIGATAA TGGCGTTGAC CGATGTCCCT TAGGTCCGAC GGAAACTGGT CCTGACCCGA AGACCCGCGT AGTGGGCGGGT GAGCATGGCG TTACCGAGAC CTGCACTATT ACCGCAACTG GCTACAGGGA ATCCAGGCTG CCTTTGACCA GGACTGGGCT TCTGGGCGCA TCACCCGCCA CTCGTACCGC AATGGCTCTG 2501
 - CCTGGCCTAC AAGCTGCTCA TCCAGACTGG AGACGCCCCAG GAGCCTCTGG ATTTCAGCCA GGTTGGGAGA GGGCTGGAGG GGTCCACTAG rectaecece geaecegate tresagaast aggretgaee tergegggte eteggagaee taaagteggt ecaaecetet eeggaeetee ceaggigate AGGATGGGGC 2601
- 2701 TACAGGGGCT GCAGGCCTCC TGGGCCCAGG CCTTCAGCCC TCTCTGCCTC TGCAGCTGAC CACAAGGAAG CTGGTGGACA GAGAGGGACT GATTCCACCC ATGTCCCCGA CGTCCGGAGG ACCCGGGTCC GGAAGTCGGG AGAGACGGAG ACGTCGACTG GTGTTCCTTC GACCACCTGT CTCTCCCTGA CTAAGGTGGG GAATGGCTGC
 - CTTACCGACG GAGCTCTTCT ACATGGGGCT GACCGTGTGG GTGAGCAGTG ACCCCCTGGG TCTGGCAGCC TCACAGGCCA ACTTCTACCC CCCACCTCCT CTCGAGAAGA TGTACCCCGA CTGGCACACC CACTCGTCAC TGGGGGACCC AGACCGTCGG AGTGTCGGGT TGAAGATGGG GGGTGGAGGA 2801
 - 2901 ACGACAAATA CGACACCACG GGGGAGAACC TTCGCAGTGA GTCTTGGGGG GAGCTCGGCA AGAGCCTCAG CCTCGCCCAC ACAAGCCCTG AGCCTGAGGC rectental ecteregree eceptoring arecendat cagaaceee etegageegt teteggagie ggagegggtg tettegggae tegaacieg AGTTTGCCCA
 - GGACGGGTGA GACGGGGACAC GAGTGGCGGG ACAGGGAGAG GGAGAAGAGG GAAGGGGGTGTCA GGGCGGTCGA GTCGGGAACC TCAAACGGGT censeceaer enseceests encaesses nancenene cenenteres entesecence echecadar ecosecaser casecentss 3001

FIG. 10C

CAAGGGGAAG GACGACGCAC CGGAGGTCTT CTGACGTCTG AAACACCTCC GGTAGCTCCC CCGGGCCCGT CGTACGCGTC TCCGGCCGGT CCGACCCCAC 3101 GTTCCCCTTC CTGCTGCGTG GCCTCCAGAA GACTGCAGAC TTTGTGGAGG CCATCGAGGG GGCCCGGGCA GCATGCGCAG AGGCCGGCCA GGCTGGGGTG

GTGCGGATGG GGTCGCCGAG GGGGAAGGAG AAGACCCTTG TCATAGACCC GGACGCCGCG ACGAAGGACG ACCGGCAGAC GTAGGACGAC CACACGTGAA rescentre carectette ererecatr CCCTTCCTC TICIGGAAC AGTAICTGGG CCTGCGGCGC TGCTICCTGC CCAGCGGCTC CACGCCTACC 3201

AGGAGCAGAC ACGAGACGAC GAGGAGTTGG GGACCTGCCG ACCGGAGTAT CACTCACGAA CGTCCTCACC CCTGTCTCTG TGGGGTGGGA AGGGACGGGT TCCCTGCCCA CCTGGACGGC TGGCCTCATA GTGAGTGCTT GCAGGAGTGG GGACAGAGAC ACCCCACCCT CTCCTCAACC recreators recreated 3301

CGGACAGTAG GGAGGACGGT CCTCGGGAGA CACTCGGGAC AGAGGGAGTC CACGACCAGG ACCGCTACTA CTGTCACCTT GAGAAACCAT AGTACCCAAA TGGCGAIGAI GACAGIGGAA CICITIGGIA ICAIGGGIII GTGCTGGTCC GCCTGTCAIC CCTCCTGCCA GGAGCCCTCT GTGAGCCCTG TCTCCCTCAG 3401

GAGCACGGGC GGACCCGTAG TTCGACTCAC GGTAGGGGCA CCACTAGGAA CACCGGAGAC ATCCGTAACC GCAACTCAAG TGTCAGGTGC ACCGAGACCA CTCGTGCCCG CCTGGGCATC AAGCTGAGTG CCATCCCCGT GGTGATCCTT GTGGCCTCTG TAGGCATTGG CGTTGAGTTC ACAGTCCACG TGGCTCTGGT

3501

CTGGGTGGAC CCCTGGTTAG TCGACTAAGT CATAAAGTTGT GTATAACAAG TTCGGGGATG ATACACGATC CATGATAAAT TCTTAAACCC GACCCACCTG ACCCCGGGGA GGGACCAATC AGCTGATTCA GTATTCAACA CATATTGTTC AAGCCCCTAC TATGTGCTAG GTACTATTTA AGAATTTGGG PGGGGCCCT 3601

GTEGTEGCTC ATTCCTGTAA TCCCAGCACT TTGGGAGGCC GAGGCGGGTG GATCACCTGA GGTCGGGAGT TCGAAACCAG CCTGGCCAAC ATGGTGAAAC CACCACCGAG TAAGGACATT AGGGTCGTGA AACCCTCCGG CTCCGCCCAC CTAGTGGACT CCAGCCCTCA AGCTTTGGTC GGACCGGTTG TACCACTTTG 3701

CTCCGACTCC GTCTTAACGA ACTTGGACCC TGAACCTGGG AAAAATTAG CCAGGCGTGG TGGCACATGC CAGTAGTCCC AGCTACTTTG GAGGCTGAGG CAGAATTGCT TCGATGAAAC GGACAGAAAT GATTTTATG TTTTTAATC GGTCCGCACC ACCGTGTACG GTCATCAGGG CCTGTCTTTA CTAAAAATAC 3801

AGGCGAAGGT TGCAGTGAGC TGAGATCGTG CCATTGCACT CCAGCCTGGG CAACAAGAGT GCAACTCTCC GTCTCAAAAA AAAAAAAA AAGGGCGGCC ICCGCTICCA ACGICACICG ACICIAGCAC GGIAACGIGA GGICGGACCC GITGITCICA CGIIGAGAGG CAGAGIITIT IITIIIII IICCCGCCGG 3901

4001 GCGA

CGCT

FIG. 10D

~ Clone 16.1 human patched > length: 2082 bp

(SEQ ID NO:9)

- renceacede ecencaater enecedence acertecen cerecedener accarcaace ereceaert GAGCCTGAAG TCCTAGCTGG TICCOGÉATG ACTOGATOGO COCCOTOAG AGAGOTGOCO COGAGITACA CACCOCOAGO TOGAACOGOA GCACOCOAGA AAGGÉCGTAC TGAGCTAGCG GCGGGAGTC
- CGAGGTGAGA CCGAAGCACG AATGAAGGTC CCGGACGAGA AGAGAGCCC TACGCCCTAG GTCTCTGTAA CACCGTTTCA CGAGAAAGAC CCTGACAACC GTGGCAAAGT CAGAGACATT GGCCTGCTCT TCTCTGGG ATGCGGGATC 101 GCTCCACTCT

GCTCTTTCTG GGACTGTTGG

- AGGAGCTGCA GCCCACTCGG TCCTCGACGT CGGGTGAGCC GGAAACCCCG GGACCGTAAT CCAGAGGCGT ACCGGTAATA ACTCTGTTTG AACCTTGTCG AGACCCATCT TCACCCGTCG TGGCCATTAT TGAGACAAC TTGGAACAGC TCTGGGTAGA AGTGGGCAGC commesse cerescanta seretecsea 201
- GAGGGAGAGA ACATCCTCAC ACCCGAAGCA AATGIGGITC CICITICGACC CCCTCCTCCG ACGIATGIGG AGAGICTACG ACTAIGICIG GCGIGCGGIC CICCCICICI IGTAGGAGIG IGGGCITICGI CGCACGCCAG TGCATACACC TCTCAGATGC TGATACAGAC TTACACCAAG GAGAAGCTGG GGGAGGAGGC 301
- AAGTCAGGAG GAACCGGAGG TGGAGGTCCG TCGGGAGTGA CGGTCATTC AGGTTCATAG TGAGATACCC TTCAGGACCC TAAACTTGTT TTAGACGATG TTCAGTCCTC AATCTGCTAC ATTTGAACAA AAGTCCTGGG ACCTCCAGGC AGCCCTCACT GCCAGTAAAG TCCAAGTATC ACTCTATGGG CITGGCCICC 401
- AAGGGGAATA ACTITIACCT TACTAACTCA CCTACTAACT CTTCGACAAA GGCACGCACT AGGAGTGGGG GGAGCTGACG AAGACCCTCC TTCTGGGAGG GGATGATIGA GAAGCIGITT CCGIGCGIGA ICCICACCCC CCICGACIGC TICCCCTIAI IGAAAAIGGA AIGATIGAGI 501
 - GGTTCCCCCG AGGCGGATGG ACGGGCCGGC GGGCCTATAG GTCACCTGGT TGGACCTAGG TCTCGTCGAC GACCTCCTCG ACCCAGGGAA ACGGAGGAAA TOCCCGGCCG CCCGGATATC CAGTGGACCA ACCTGGATCC AGAGCAGCTG CTGGAGGAGC TGGGTCCCTT TGCCTCCTT CCAAGGGGGC 601
- CCACTGCCCA CCTAGTGCCC TOTGITCOGT GICCACCOGG ICCGGAIGCA COCCGCOGG ACAGACGIGG GACTACIGGA GGIGACGGGI GGAICACGGG CAGGIGGGC AGGCCTACGT GGGCGGCCC TGTCTGCACC CTGAIGACCT AGACAAGGCA CCCTCGACGA GGGAGCTGCT GAGGGCTTCC CTCCCGAAGG 701
 - TCCTTAACGA CCAACCATCA CAGCAGGCAG GÇTCCCAATG TGGCTCACGA GCTGAGTGGG GGCTGCCATG GCTTCTCCCA CAAATTCATG CACTGGCAGG GGTTGGTAGT GTCGTCCGTC CGAGGGTTAC ACCGAGTGCT CGACTCACCC CCGACGGTAC CGAAGAGGGT GTTTAAGTAC GTGACCGTCC 801

AGGAATTGCT

CGACCCTCCG TACCGGTCTC TGGGGGTTCC TCTCGACGAC TCCCGTCTCC GGGACGTCTC GTGGAAGAAC GACTACTCAG GGGCGGTCGA CATGCTCGTA ccccccccc graceagcar GCTGGGAGGC ATGGCCAGAG ACCCCCAAGG AGAGCTGCTG AGGGCAGAGG CCCTGCAGAG CACCTTCTTG CTGATGAGTC 901

FIG. 11A

- CTTTGTGCAG CTGGCCCAGG AAGGCCCCAC TGATAGTCTG TGTACTGTAA CCGACCTCAC TCCTCGTCCG GTCGTGTCAC GATGTTCGGA CCGTCGCCGC GAAACACGTC GACCGGGTCC TICCEGEGITE ACTATCAGAC ACATGACATT GECTGGAGTG AGGAGCAGGC CAGCACAGTG CTACAAGCCT GGCAGCGGCG 1001
 - TOCCAGOAGA TOCATGOOTT CTOCTOCACO ACCOTGGATA ACATOCTGCA TGOGTTOTOT GAAGTCAGTG CTGCCGTGT TCCGGGACGG ACTCTTGCGA AGGGTCGTCT AGGTACGGAA GAGGAGGTGG TGGGACCTAT TGTAGGACGT ACGCAAGAGA CTTCAGTCAC GACGGGCACA AGGCCCTGCĆ 1101
- GGTGĞĞAGGC TATCTGCTCA TGCTGGGCTA TGCCTGTGTG ACCATGCTGC GGTGGGACTG CGCCCAGTCC CAGGGTTCCG TGGGCCTTGC CGGGGTACTG CCACCTCCG ATAGACGAGT ACGACGGAT ACGGACACAC TGGTACGACG CCACCCTGAC GCGGGTCAGG GTCCCAAGGC ACCCGGAACG GCCCATGAC 1201
 - GACCACCGGG ACCGCCACCG GAGTCCGGAA CCCGAGACAC GGGACGAGCC GTAGTGGAAG TTACGACGGT GATGGGTCCA CGACGGGAAG AACCGAGACC CATCACCITC AATGCTGCCA CTACCCAGGT GCTGCCCTTC TTGGCTCTGG CIGGIGGCCC IGGCGGIGGC CICAGGCCTIT GGGCTCTGTG CCCTGCTCGG 1301
- GECGAGTGTC TGCAGCGCAC CCTACTGCAT AAGGACGACC GCGTACGGAA GTGTCTCCGA GACGGACCGT GGGGAGAGGT CCTCGCGTAC CCGCTCACAG ACGTCGCGTG GGAGCGCATG GAATCGGCGT GGATGACGTA TTCCTGCTGG CGCATGCCTT CACAGAGGCT CTGCCTGGCA CCCCTCCCA CTTAGCCGCA 1401
 - CTTACAGCCA CCCGTGGTCA CAGCATGAGT GTAGGTAGTT GTTGTACCGG CGGAAGGAGT ACCGACGGGA GCAAGGGTAG GGACGCGACG CTCGGAAGAG GAATGTCGGT GGGCACCAGT GTCGTACTCA CATCCATCAA CAACATGGCC GCCTTCCTCA TGGCTGCCCT CGTTCCCATC CCTGCGCTGC GAGCCTTCTC 1501
- GGACCIACGG CGGCGCCACT GCAGGGCCT TGATGTGCTC TGCTGCTTCT CCAGTCCCTG CTCTGCTCAG GTGATTCAGA TCCTGCCCCA AGGAGTEGGA CCTGGATGEC GECGEGTGA CGGTEGEGGA ACTACAEGAG AEGAEGAAGA GGTEAGGGAE GAGAEGAGTE CAETAAGTET AGGAEGGGT TCCTCAGCCT 1601
- GGAGCTGGGG GACGGGACAG TACCAGTGGG CATTGCCCAC CTCACTGCCA CAGTTCAAGC CTTTACCCAC TGTGAAGCCA GCAGCCAGCA TGTGGTCACC CCTCGACCCC CTGCCCTGTC ATGGTCACCC GTAACGGGTG GAGTGACGGT GTCAAGTTCG GAAATGGGTG ACACTTCGGT CGTCGGTCGT ACACCAGTGG GGAGCTGGGG 1701
 - ATCCTGECTE ECCAAGECEA CETGGTGEE CEACETTETG ACCEAETGGG ETETGAGETE TTEAGECETG GAGGGTECAE AEGGGACETT ETAGGECAAG IAGGACGGAG GGGTTCGGGT GGACCACGGG GGTGGAGAC TGGGTGACCC GAGACTCGAG AAGTCGGGAC CTCCCAGGTG TGCCCTGGAA GATCCGGTCC 1801
 - TICCETCIIC CGICGGACGI ICAGGGACGG GACACGGGCG ACCTIAGAAC GGGTAAAGCG GGGCCTIAAG GACGICGGGC CCCCIAGGIG CCCGGAATTC CTGCAGCCCG GGGGATCCAC CCCATTTCGC AGGAGGAGAC AAGGCAGAAG GCAGCCTGCA AGTCCCTGCC CTGTGCCCGC TGGAATCTTG recreaters 1901
- ATCAAGATCT CGCCGGCGGT GGCGCCACCT CGAGGTCGAA AACAAGGGAA ATCACTCCCA ATTAACGCGC GAACCCATAG AA Ţ TAGITCIAGA GCGGCCGCCA CCGCGGTGGA GCTCCAGCTT TTGITCCCTT TAGIGAGGGI TAATIGCGCG CITGGGIAIC 2001

FIG. 11B